

WHAT IS CLAIMED IS:

1. A method of treating an individual suffering from a cancer comprising administering to the individual a therapeutically effective amount of a composition comprising an inhibitor or antagonist of reverse transcriptase encoded by L-1 (LINE-1) retrotransposon in cells of the individual, wherein the inhibitor or antagonist blocks lengthening of telomeres in telomerase negative cells.
2. The method of claim 1, wherein the inhibitor or antagonist of the reverse transcriptase comprises an antisense sequence, an inorganic compound, an organic compound, a peptide or a small molecule.
3. The method of claim 1, wherein the antisense sequence is capable of hybridizing with a nucleic acid encoding the reverse transcriptase.
4. The method of claim 1, wherein the nucleic acid encoding the reverse transcriptase comprises an RNA transcribed from the DNA.
5. The method of claim 1, wherein the antisense sequence comprises a chimeric RNA-DNA oligonucleotide.
6. The method of claim 1, wherein the organic compound is a nucleoside analog.
7. The method of claim 1, wherein the organic compound is a nucleoside analog, which is 3'-azido-2',3'-dideoxythymidine (AZT), 2',3'-dideoxyinosine (ddI), 2',3'-didehydro-3'-deoxythymidine (d4T) ganciclovir or valganciclovir, or a combination thereof.

8. The method of claim 1, wherein the cancer is osteosarcoma, breast carcinoma, ovarian carcinoma, lung carcinoma, adrenocortical carcinoma or melanoma.

9. The method of claim 1, wherein the composition is administered orally, parenterally, subcutaneously, intramuscularly, intravascularly or topically.

10. A method for treating a cancer in a human, wherein the cancer is due to cells showing alternative lengthening of telomeres induced or mediated by L-1 (LINE-1) retrotransposon encoded reverse transcriptase in said cells of the human, the method comprising administering a therapeutically effective amount of a composition comprising one or more nucleoside analogs, or a pharmaceutically acceptable salt thereof, to the human suffering from the cancer.

11. The method of claim 10, wherein said nucleoside analogs are at least one selected from the group consisting of: 3'-azido-2',3'-dideoxythymidine (AZT), 2',3'-dideoxyinosine (ddI), 2',3'-didehydro-3'-deoxythymidine (d4T) ganciclovir and valganciclovir.

12. The method of claim 10, wherein the cancer is osteosarcoma, breast carcinoma, ovarian carcinoma, lung carcinoma, adrenocortical carcinoma or melanoma.

13. The method of claim 10, wherein the composition is administered orally, parenterally, subcutaneously, intramuscularly or intravascularly.

14. The method of claim 10, wherein a composition comprising two or more said nucleoside analogs are administered.

15. The method of claim 10, wherein the one of said nucleoside analogs administered is from about 10 mg/kg of body weight to about 100 mg/kg of body weight per day.

16. A method of interfering with lengthening of telomeres in telomerase negative tumor cells, the method comprising administering to the cells an effective amount of an inhibitor or antagonist of reverse transcriptase encoded by L-1 (LINE-1) retrotransposon in the cells.

17. The method of claim 16, wherein the inhibitor or antagonist of the reverse transcriptase comprises an antisense sequence, an inorganic compound, an organic compound, a peptide or a small molecule.

18. The method of claim 16, wherein the antisense sequence is capable of hybridizing with a nucleic acid encoding the reverse transcriptase.

19. The method of claim 16, wherein the nucleic acid encoding the reverse transcriptase comprises a DNA, an RNA transcribed from the DNA or a cDNA reverse transcribed from the RNA.

20. The method of claim 16, wherein the antisense sequence comprises a chimeric RNA-DNA oligonucleotide.

21. The method of claim 16, wherein the organic compound is a nucleoside analog.

22. The method of claim 16, wherein the organic compound is a nucleoside analog, which is 3'-azido-2',3'-dideoxythymidine (AZT), 2',3'-dideoxyinosine (ddI),

2',3'-didehydro-3'-deoxythymidine (d4T) ganciclovir or valganciclovir or a combination thereof.

23. The method of claim 16, wherein the cancer is osteosarcoma, breast carcinoma, ovarian carcinoma, lung carcinoma, adrenocortical carcinoma or melanoma.

24. A method of preventing or inhibiting the growth of a telomerase negative cell, the method comprising:

contacting the cell with a nucleoside analog; or
transfected the cell with a construct capable of expressing human L1RT antisense sequence that is substantially or fully complementary to a subsequence of a nucleic acid necessary for encoding L1RT enzyme.

25. The method of claim 24, wherein the cell is contacted with a nucleoside analog at a concentration of 0.2 μ M.

26. The method of claim 24, wherein the nucleic acid is an mRNA.

27. The method of claim 24, wherein the nucleic acid is a human L1RT open reading frame.

28. The method of claim 27, wherein the nucleic acid encodes a protein comprising SEQ ID NO:

29. The method of claim 24, wherein the nucleoside analog is 3'-azido-2',3'-dideoxythymidine (AZT).

30. The method of claim 24, wherein the antisense sequence is a DNA oligonucleotide, a 2'-O methyl oligonucleotide, a peptide nucleic acid oligonucleotide or a phosphorothioate oligonucleotide.

31. The method of claim 30, wherein the antisense L1RT nucleic acid has the nucleotide sequence comprising SEQ ID NO:1.

32. The method of claim 24, wherein the antisense sequence is about 8 to about 50 nucleotides in length.

33. The method of claim 32, wherein the antisense sequence is about 15 to about 25 nucleotides in length.

34. The method of claim 24, wherein the cell is contacted with two or more antisense sequences fully complementary to different subsequences of the nucleic acid.

35. The method of claim 24, wherein the antisense sequence is part of a ribozyme.

36. The method of claim 24, wherein the telomerase negative cell is a cancer cell, wherein the cancer cell is selected from the group consisting of osteosarcoma, breast carcinoma, ovarian carcinoma, lung carcinoma, adrenocortical carcinoma or melanoma.

37. A method for interfering with L1RT activity in a system competent to perform L1RT transcription, comprising providing to the system an amount of a nucleoside analog or an antisense compound effective to interfere with L1RT activity in the system, wherein the system is a cell growing in vitro or in vivo.

38. The method of claim 37, wherein the nucleoside analog is 3'-azido-2',3'-dideoxythymidine (AZT), 2',3'-dideoxyinosine (ddI), 2',3'-didehydro-3'-deoxythymidine (d4T), ganciclovir or valganciclovir, or a combination thereof.

39. A method for prevention of a cancer in a person in need thereof, wherein the cancer is due to cells showing alternative lengthening of telomeres induced or mediated by L-1 (LINE-1) retrotransposon encoded reverse transcriptase in said cells of the person, the method comprising administering to said person a therapeutically effective amount of a composition comprising one or more nucleoside analogs, or a pharmaceutically acceptable salt thereof.

40. The method according to claim 39, wherein said cancer is selected from the group consisting of: osteosarcoma, breast carcinoma, ovarian carcinoma, lung carcinoma, adrenocortical carcinoma and melanoma.

41. A composition comprising: a polynucleotide capable of encoding a nucleic acid segment capable of interfering with L-1 (LINE-1) retrotransposon activity in cells.

42. The composition of claim 41, wherein the nucleic acid segment comprises SEQ ID NO:1.

43. An isolated host cell comprising the composition of claim 41.

44. The isolated cell of claim 41, wherein the cell is human cell.

45. The isolated cell of claim 41, wherein the cell is a cancer cell.

46. A method of selecting a compound capable of shortening telomeres in telomerase negative cancer cells, the method comprising:

administering a test compound to said cells;
evaluating anti-L-1 (LINE-1) retrotransposon activity of the test compound or evaluating whether the compound down-regulates expression of reverse transcriptase encoded by L-1 retrotransposon in said cells; and
selecting the compound that exhibits anti-L-1 retrotransposon activity down-regulates the reverse transcriptase expression.

47. The method of claim 46, wherein the step of evaluating comprises testing for telomere shortening or G2 arrest in said cells or apoptosis of said cells.

48. The method of claim 46, wherein said cells are either in vitro cultured cells or in a non-human animal model.

49. The method of claim 46, wherein the animal model is selected from the group consisting of a mouse, a rat, a rabbit, a pig, a cow, a monkey and a guinea pig.

50. A method of detecting presence of cancerous cells in a cell sample that is telomerase negative, the method comprising:

contacting said sample with an inhibitor or antagonist of reverse transcriptase encoded by L-1 (LINE-1) retrotransposon; and
testing for cells exhibiting telomere shortening or G2 arrest in said cells or apoptosis of said cells.

51. A method of detecting cells capable of pathologically proliferating in a tissue of a mammal, comprising:

obtaining a sample of cells from the tissue
contacting the sample of cells with a nucleic acid probe that is substantially complementary or fully complementary to a subsequence of an L1RT mRNA, or an antibody specific to L1RT reverse transcriptase; and

detecting L1RT expression in said cells.

52. The method of claim 51, wherein the nucleic acid probe comprises a detectable moiety.

53. The method of claim 52, wherein the detectable moiety is a radioisotope, a fluorescent molecule, biotin or digoxigenin.

54. The method of claim 51, wherein the nucleic acid probe comprises a sequence selected from the group consisting of: 5'-CCA GAG ATT CTG GTA TGT GGT GTC TTT GTT-3' (SEQ ID NO:2), 5'-CTT TCT CTT GTA GGC ATT TAG TGC TAT AAA-3' (SEQ ID NO:3), 5'-CTC TTG CTT TTC TAG TTC TTT TAA TTG TGA-3' (SEQ ID NO:4), 5'-CTT CAG TTC TGC TCT GAT TTT AGT TAT TTC-3' (SEQ ID NO:5) and 5'- TCC TGC TTT CTC TTG TAG GCA -3' (SEQ ID NO:6).

55. A method of inhibiting polymerase activity of L-1 (LINE-1) retrotransposon or inducing apoptosis in isolated cells or tissues expressing said retrotransposon comprising contacting said cells or tissues with a composition comprising at least one nucleoside analog or an antisense sequence or both so that polymerase activity is inhibited.

56. The method of claim 55, wherein said nucleoside analog is 3'-azido-2',3'-dideoxythymidine (AZT), 2',3'-dideoxyinosine (ddI), 2',3'-didehydro-3'-deoxythymidine (d4T) ganciclovir or valganciclovir, or a combination thereof.

57. The method of claim 55, wherein the an antisense sequence is selected from the group consisting of: 5'-CCA GAG ATT CTG GTA TGT GGT GTC TTT GTT-3' (SEQ ID NO:2), 5'-CTT TCT CTT GTA GGC ATT TAG TGC TAT AAA-3' (SEQ ID NO:3), 5'-CTC TTG CTT TTC TAG TTC TTT TAA TTG TGA-3' (SEQ ID NO:4), 5'-

CTT CAG TTC TGC TCT GAT TTT AGT TAT TTC-3' (SEQ ID NO:5) and 5'- TCC TGC TTT CTC TTG TAG GCA -3' (SEQ ID NO:6).

58. A kit for detecting pathologically proliferating cells comprising a nucleic acid probe that is substantially or fully complementary to a subsequence of an L1RT mRNA.

59. The kit of claim 58, wherein the nucleic acid probe comprises a detectable moiety.

60. The kit of claim 59, wherein the detectable moiety is a radioisotope, a fluorescent molecule, biotin or digoxigenin.

61. The kit of claim 58, wherein the nucleic acid probe comprises a sequence selected from the group consisting of: 5'-CCA GAG ATT CTG GTA TGT GGT GTC TTT GTT-3' (SEQ ID NO:2), 5'-CTT TCT CTT GTA GGC ATT TAG TGC TAT AAA-3'(SEQ ID NO:3), 5'-CTC TTG CTT TTC TAG TTC TTT TAA TTG TGA-3' (SEQ ID NO:4), 5'-CTT CAG TTC TGC TCT GAT TTT AGT TAT TTC-3' (SEQ ID NO:5) and 5'- TCC TGC TTT CTC TTG TAG GCA -3' (SEQ ID NO:6).